Closed System Administration of Fluothane®*

GRANT FLETCHER, *M.D.*, Monterey

• **Fluothane® was administered in a closed system to 518 surgical patients. No morbidity or mortality was attributable to using Fluothane by this technique. Requisites for safe administration of Fluothane in a closed system include (1) an understanding of the basic concepts of closed systems, (2) a vaporizer outside of the breathing circuit which will accurately and dependably deliver precise amounts (in a range of 10 to 60 cc.) of oxygen saturated with Fluothane, and (3) a thermally stable vaporizer.**

If the demands for safe operation are met, Fluothane anesthesia with the closed system technique becomes the simplest, most economical and effective method for general anesthesia in adults.

THE INTRODUCTION of Fluothane® by Raventos[14] and Johnstone[9] in 1956 made available a potent nonexplosive anesthetic agent. It was made available for use in the United States in 1958. Many clinical and laboratory reports have confirmed its usefulness, advantages and hazards. Ability to control the inspired concentration of Fluothane over a very narrow range is the most critical factor in its safe administration. In order to meet this requirement most investigators have stressed the use of nonrebreathing or partial rebreathing systems, and special vaporizers have been developed for this purpose.[8,13,16] The objections to these high flow inhalation techniques are that they are costly and wasteful of gases and Fluothane, that they are too complex and that the constantly full anesthesia bag makes it difficult to judge the patient's respiratory exchange. Since other potent anesthetic agents are administered safely in closed rebreathing systems, there would not appear to be any reason why Fluothane could not also be administered in this manner. This paper reviews the author's experience with administration of Fluothane in a completely closed rebreathing system in 518 consecutive cases.

METHODS

Patients were premedicated with scopolamine (0.2 to 0.4 mg.) and in most instances 25 to 50 mg. of meperidine. In elderly patients, atropine was sometimes substituted for scopolamine. Thiopental sodium (75 to 250 mg.) intravenously was used to facilitate induction, and was followed by a 4-liter flow of 2 to 4 per cent Fluothane in oxygen. Surgical anesthesia was usually achieved in 3 to 7 minutes. Single doses of succinylcholine (30 to 60 mg.) or Flaxedil®† (up to 0.5 mg. per pound of body weight) were used only to facilitate tracheal intubation or relaxation for upper abdominal operations. At the completion of induction or intubation, the oxygen flow was reduced to basal metabolic requirements (100 to 250 cc. per minute) with Fluothane added as required. Respirations were manually assisted in most patients.

Foregger anesthetic machines with "copper kettles"[12] and circle filters of jumbo type were used. Oxygen flowmeters to the "copper kettles" were specifically selected to provide easy readability, in increments of 5 cc., of flows from 5 to 80 cc. per minute, and increments of 25 cc. from 80 cc. to 350 cc. per minute. Performance of the vaporizers was monitored with an oxygen analyzer (Beckman) and a thermistor indicating thermometer. During vaporization the temperature of the "kettles" did not vary significantly from room temperature, and the outflow at 20°C. contained 34 per cent Fluothane. This is in agreement with the findings of Feldman and Morris for similar apparatus.[6]

Blood pressure was estimated by the oscillometric method. Cardiac rate and rhythm were continuously monitored with a cardioscope in 399 cases, and with a stethoscope in the remainder.

CLINICAL MATERIALS

The patients in this study were dealt with in the author's private practice of anesthesiology in two small general hospitals. Included were all patients to whom Fluothane was administered in a closed system during the years 1959 and 1960. During this period the only patients receiving general anesthesia by other techniques or agents were children under 10 years of age, obstetrical patients and patients whose operations were expected to last less than 30 minutes.

The patients ranged in age from 4 to 92 years and were classified according to physical status

*A brand of 1,1,1, Trifluoro-2,2, bromochlorethane.

Presented before the Section on Anesthesiology at the 90th Annual Session of the California Medical Association, Los Angeles, April 30 to May 3, 1961.

†Flaxedil is a brand of gallamine triethiodide.

TABLE 1.—*Data on Patients Undergoing Fluothane Anesthesia in a Closed System, by Age and Physical Status (Risk).*

Age	Number of Patients
0 to 5 years	2
6 to 10 years	8
11 to 20 years	56
21 to 30 years	56
31 to 40 years	92
41 to 50 years	103
51 to 60 years	77
61 to 70 years	83
Over 70 years	41
Total	518

Physical Status of Patients	
A.S.A. Classification	Number of Patients in Class
1	219
2	174
3	42
4	0
5	61
6	22
	518

(American Society of Anesthesiologists classification), 1 through 6 (Table 1). Preoperative complications which did not preclude the use of general anesthesia, did not preclude the use of Fluothane. The most common preoperative complications were respiratory diseases, and secondly diseases of the cardiovascular system. Hypovolemia was not considered a contraindication to the use of Fluothane.

Surgical procedures of all types, with the exception of obstetrical operations, on all sites of the body were included in the series (Table 2). The duration of anesthesia ranged from 20 minutes to 8 hours; in most cases it was between 1 and 3 hours (Table 3).

RESULTS

Induction. Induction was smooth, rapid and noticeably lacking in laryngospasm, stridor or excess secretions. Surgical levels of anesthesia were achieved in 3 to 7 minutes, but pharyngeal and laryngeal reflexes were obtunded early. Tracheal intubation could be carried out in 5 to 10 minutes with Fluothane alone, and in a shorter time if succinylcholine or Flaxedil was used. The time available for tracheal intubation with Fluothane alone is rather brief, and the use of relaxants eases the job and reduces the incidence of "bucking" on the tube.

Maintenance. During maintenance the flow of oxygen was set at the estimated basal metabolic requirements of 100 to 250 cc. per minute, and oxygen with Fluothane was added from the "copper kettle" as indicated by clinical demand. In the vast majority of patients a flow of 20 to 40 cc. of oxygen through the "kettle" would suffice to provide a steady level of surgical anesthesia throughout operation. Maintenance rates varied, however, from 10 cc. to 60 cc. per minute. The only consistent indicator of deepening anesthesia was a fall in blood pressure, and even this was misleading if there was minimal surgical stimulation. In general, changes in the rate of Fluothane administration were minimal once operation was under way. Excellent operating conditions were provided in every case, and it was never necessary to abandon the use of Fluothane or add another anesthetic agent. Fluothane was discontinued during the last 20 minutes of operation or after the peritoneum was closed. Patients generally had return of pharyngeal reflexes by the end of the procedure and responded to vocal commands within the first postoperative half hour.

TABLE 3.—*Duration of Anesthesia with Fluothane in a Closed System.*

Duration of Anesthesia	Patients	
	Number	Per Cent
0 to ½ hour	8	1.5
½ to 1 hour	82	16
1 to 2 hours	191	37
2 to 3 hours	157	30
3 to 4 hours	52	10
Over 4 hours	28	5.5
Total	518	100.0

Muscular relaxation. Sufficient relaxation for tracheal intubation and for all operative procedure except in the upper abdomen could readily be produced with Fluothane alone. A saving of about 4 minutes in the induction to intubation time could be gained with the use of relaxant drugs, and therefore 215 of the 288 patients intubated received such an agent (Table 4).

Succinylcholine in a single dose of 30 to 60 mg. was given before intubation in cases in which not much relaxation would be required for the op-

TABLE 2.—*Data on Patients Undergoing Fluothane Anesthesia in a Closed System, as to Surgical Service and Site of Operation.*

	Head Neck	Trunk	Thorax	Abdomen	Perineum	Extremity	
SERVICE:	142	75	24	171	32	74	Totals
Eye	5	....	....	....	....	....	5
ENT	99	....	....	....	....	....	99
Plastic	13	4	....	....	....	11	28
Neurosurgical	10	9	....	....	....	....	19
Urological	....	7	....	2	22	....	31
General	15	54	4	142	3	17	235
Thoracic	....	....	20	....	....	....	20
Orthopedic	....	1	....	....	....	46	47
Gynecological	....	....	....	27	7	....	34

TABLE 4.—*Use of Tracheal Intubation and Muscle Relaxants as Related to Site of Operations in Patients Undergoing Fluothane Anesthesia in a Closed System.*

Site of Operation	Number of Patients	Number Intubated	Succinylcholine	Flaxedil
Head-neck	142	142	76	3
Trunk	75	19	8	6
Thorax	24	24	6	12
Abdomen	171	98	14	86
Perineum	32	0	0	3
Extremity	74	5	4	0
Totals	518	288	108	110

TABLE 5.—*Relationship of Age to the Occurrence of Arterial Systolic Hypotension with a Fall of Greater than 25 per cent in Systolic Pressure.*

Age of Patients	Number of Patients	Number with Hypotension	Per Cent with Hypotension
0 to 10 years	10	0	0
11 to 20 years	56	0	0
21 to 30 years	56	3	5
31 to 40 years	92	4	5
41 to 50 years	103	8	8
51 to 60 years	77	14	18
61 to 70 years	83	25	33
Over 70 years	41	9	20
Total	518	63	12% (Average)

eration, and Flaxedil in single doses of less than 0.5 mg. per pound of body weight was administered if the procedure was to necessitate considerable relaxation. Of 110 patients receiving Flaxedil, 95 had upper abdominal or thoracoabdominal operations. The tachycardia from these doses of Flaxedil was helpful in reducing the tendency toward bradycardia due to Fluothane. Pulse rates over 120 per minute were rarely seen and usually subsided within 20 minutes.

Repeated doses of either Flaxedil or succinylcholine were not given, and the effect of the relaxant was completely gone by the termination of the procedure. Antagonists were never indicated or used, and no cases of postanesthetic muscle depression were noted. Closure of abdominal incisions was possible with Fluothane alone in every case.

Secretions. There was a notable lack of salivary and bronchial secretions, as is usual with Fluothane anesthesia. The extreme dryness of the mucosa required special attention to the lubrication of airways to prevent mucosal tearing. Need for preoperative and early postoperative suction was almost eliminated.

Respiratory effects. In levels of anesthesia used in this series there was an apparent decrease in spontaneous minute ventilation except in very light levels. There was a tendency toward tachypnea when surgical stimulation was severe. Assisted or controlled ventilation was used in most patients throughout anesthesia. Posthypercapnic hypotension was not observed.

Patients with emphysema or asthma tolerated Fluothane anesthesia well. Bronchospasm present before induction usually disappeared during Fluothane anesthesia. In no case did bronchospasm appear or get worse during anesthesia.

Cardiovascular effects. A decrease in systolic blood pressure of 10 to 20 per cent below the preanesthetic level almost always accompanied induction. This usually rapidly reversed after intubation or upon surgical stimulation. During maintenance, the systolic blood pressure was usually stable at about 10 per cent below the preanesthetic level. Hypotension, when it occurred, usually came on gradually, except when induced by traction reflexes. Hypertension was uncommon and never persisted more than 20 minutes.

Falls in systolic pressure greater than 25 per cent of the preanesthetic level and lasting more than 5 minutes occurred in 12 per cent of the patients (Table 5). While in many instances the occurrence of hypotension per se was directly related to the concentration of the anesthetic agent, the patient's age and vascular reactivity were major factors. Profound hypotension occurred five times more frequently in patients over 60 years (24 per cent) than in patients below 60 years (5 per cent).

In a majority of cases a reduction in the concentration caused a return of systolic pressure to acceptable levels. In upper abdominal operations, severe hypotension was usually due to traction reflexes and was reversed when manipulation lessened. Atropine was given intravenously in 12 instances, but was only effective when the hypotension was associated with bradycardia from traction reflexes. Methoxamine, 5 mg. was given intravenously in three cases and was effective in reversing the hypotension when all other measures had failed. In no case did a systolic pressure stay below 70 mm. of mercury for more than 10 minutes. Patients who did have pronounced hypotension throughout a major portion of the period of anesthesia did not show evidence of "shock," and their skin remained pink, warm and dry. There were no evidences of permanent effects due to hypotensive episodes.

In all patients the systolic blood pressure was near preanesthetic levels at the termination of anesthesia. Postoperative hypotension was rare, and oliguria related to hypotension did not occur.

Bradycardia of a degree was present in most patients in surgical levels of anesthesia, unless they had received Flaxedil. Severe bradycardia (less than 48 per minute) occurred in 12 patients. In six cases it was associated with the rapid injection of succinylcholine for tracheal intubation, and in two of

the six the pulse rate was 12 per minute for about 2 minutes. In all these patients the rate returned to normal levels after intubation without specific therapy. In the remaining six cases the bradycardia was associated with visceral traction reflexes; in four instances it reverted spontaneously and in two it responded to intravenous atropine.

Electrocardiographic effects. In 399 patients the electrocardiogram was continuously monitored with a cardioscope. Downward displacement of the pacemaker intermittently was so common as to be considered routine, but no other supraventricular arrhythmia developed during anesthesia. Preexisting auricular fibrillation was not affected by Fluothane.

Ventricular arrhythmia occurred in 42 patients. In five cases the abnormality was multifocal ventricular extrasystoles, and in the remaining 37 there were either coupled ventricular extrasystoles or single extrasystoles occurring at intervals, apparently from a single focus.

In 21 cases the occurrence of ventricular extrasystoles was related to tracheal intubation, an incidence of 7 per cent of those intubated. Usually this aberration was of short duration, and regular rhythm reappeared as soon as ventilation improved and the anesthetic level deepened.

The remaining cases of ventricular arrhythmia were associated with traction reflex phenomena or underventilation or both. The effect of underventilation was dramatic, and ventricular extrasystoles in some patients could be started or stopped by altering the degree of ventilatory assistance. In only two instances was arrhythmia associated with hypotension and in both these cases it was also associated with traction reflexes. In general, arrhythmia seemed to be a benign phenomenon. In no case was drug therapy used to stop it.

The use of epinephrine solutions. Epinephrine in a 1:100,000 concentration was injected for local hemostasis in 61 patients. Volumes injected were between 5 and 10 cc. and injections were not repeated within one hour. There was no evidence in any case of a disturbance of cardiac rhythm or of any cardiovascular effect related to epinephrine.

Morbidity and mortality. There were no operating room deaths and no case of "cardiac arrest." One death within the first 24 hours after operation was due to massive cerebral anoxia during carotid endarterectomy. There were two other deaths within the first postoperative week but they were not related to the use of Fluothane or the closed system technique.

Toxic effects on the liver or kidney were not evident although the series included patients with significant liver and kidney disease.

COMMENT

During the initial period of administration of Fluothane the uptake from the inspired gases is rapid. Within 20 minutes the rate of uptake falls rapidly to a low plateau at which it is continued for many hours.[4,11] This initial rapid fall in uptake is due to the amounts needed for the saturation of the blood and of tissues high in water content. The use of rapid flow techniques of administering Fluothane during this phase serves the double purpose of providing the large volume of Fluothane required to achieve saturation without using very high concentrations, and of denitrogenating the patient before changing to the closed system.

After the initial saturation, the rate of uptake continues a steady slow rate as the Fluothane is lost from the blood into the tissues, mainly the fat.[4,11,15] Because of the high degree of transferability of Fluothane from water to oils, this outflow to the tissues will go on for at least a hundred hours, with the agent at the same concentration in the inspired air, before the saturation point of fat tissue is approached. For practical purposes of clinical anesthesia, the uptake of Fluothane during anesthesia maintenance will be steady, and addition of an equal amount of Fluothane from the vaporizer to a closed system should maintain an even level of concentration in the inspired air. Because of the small and fixed rate of outflow to the tissues, small changes in the inflow of Fluothane from the vaporizer will cause relatively large changes in concentration within a short period of time.[13]

In the average adult, the total uptake of Fluothane vapor during steady anesthesia is 15 cc. per minute at an inspired concentration of 1.5 per cent.[1,13,15] This is the amount of Fluothane vapor emitted by a "copper kettle" when 30 cc. of oxygen is flowed through it at 20°C.[6] Abajian,[1] Robson and coworkers[15] and Mushin,[13] using infrared absorption techniques of measuring Fluothane concentration, showed that with this amount of Fluothane added continuously to a closed system, the concentration of Fluothane in the inspired gas will remain constant. They found no evidence of a sudden build-up of concentration, even after several hours of administration. The author found no clinical evidence of such build-up in the present series.

Reports of sudden profound and often unexpected hypotension occurring frequently during closed system administration of Fluothane[5,7] have been the result of the use of standard vaporizers, vaporizers in the breathing circuit or vaporizers not specifically calibrated for low flow techniques. Control of the concentration of Fluothane can only be achieved if there is absolute control of the flow of gas through the vaporizer. This requires that the vaporizer be

outside the breathing circuit.[16] In order to provide for variations from patient to patient, and within the same patient during the closed system administration of Fluothane, the flow of oxygen through a "copper kettle" must be finely adjustable within a range of 5 to 60 cc. per minute.

When the necessary criteria for control are met, as detailed above, then Fluothane anesthesia in a closed system is not associated with any more frequent complications than are other techniques.[1,2,16] The incidence of hypotension is related more to the agent per se than to the technique of administration. The influence of age and of traction reflexes in the occurrence of hypotension is not limited to Fluothane; these influences are factors with any anesthetic agent. The fact that postanesthetic sequelae due to the hypotension associated with Fluothane anesthesia have not been any greater than with other anesthetic agents suggests that existing criteria for safe levels of systolic blood pressure during Fluothane anesthesia may need to be revised downward.

That there is a relationship between pharyngeal manipulation or tracheal intubation and cardiac arrhythmia has been well established. It is not surprising that the same would hold true, as the present report indicates, of Fluothane anesthesia.[10] The role of underventilation in the production of ventricular arrhythmias, as described by Black,[3] was quite evident in some patients in this series. During Fluothane anesthesia, ventricular arrhythmia seldom occurs at times of hypotension, suggesting that a high level of circulating catechol amines is necessary for its occurrence. This would be in conformity with the proven sensitization of the myocardium to catechol amines that occurs with Fluothane and other halogenated hydrocarbons.[14]

While the author does not advocate the indiscriminate use of epinephrine during Fluothane anesthesia, personal experience in this series and an additional 140 cases not included here indicates that its use is not absolutely contraindicated. Use of not more than 10 cc. of 1:100,000 epinephrine (or the equivalent of another concentration) will not result in demonstrable undesirable effects.

Finally in an era of rapidly rising costs of medical care it is gratifying to be able to introduce savings. The cost of supplying oxygen and Fluothane in a closed system is about 50 cents an hour; the cost of nitrous-oxide-oxygen Fluothane mixture at 4 liters per minute is about $2.50 an hour.

P.O. Box 569, Monterey.

REFERENCES

1. Abajian, J., Brazell, E. H., Dente, G. A., and Milles, E. L.: Experience with halothane (Fluothane) in more than five thousand cases, J.A.M.A., 171:535-540, Oct. 3, 1959.

2. Ausherman, H. M., and Adan, A.: Fluothane, So. Med. J., 52:46-52, Jan. 1959.

3. Black, G. W., Linde, H. W., Dripps, R. D., and Price, H. L.: Circulatory changes accompanying respiratory acidosis during halothane anesthesia in man, Brit. J. Anes., 31:238-246, June 1959.

4. Duncan, W. A. M., and Raventos, J.: The pharmokinetics of halothane anaesthesia, Brit. J. Anaes., 31:302-315, July 1959.

5. Evans, P. H., and Hutter, C. G.: Fluothane: Closed circuit use in 20 cases of intervertebral body spinal fusion, Anes. and Analgesia, 39:287-292, May 1960.

6. Feldman, S., and Morris, L. E.: Vaporization of halothane and ether in the copper kettle, Anesthesiology, 10:650-655, Sept. 1958.

7. Gain, E. A., and Paletz, S. G.: An attempt to correlate the clinical signs of Fluothane anesthesia with the electroencephalographic levels, Can. Anaes. Soc. J., 4:289-294, July 1957.

8. Hudon, F., Jacques, A., Clavet, M., and Houde, J.: Clinical observations on Fluothane anesthesia, Can. Anaes. Soc. J., 4:221-234, July 1957.

9. Johnstone, M.: The human cardiovascular response to Fluothane anesthesia, Brit. J. Anaes., 28:392-410, Sept. 1956.

10. Johnstone, M., and Nisbet, H. A.: Ventricular arrhythmia during Fluothane anesthesia, Brit. J. Anaes., 33:9-16, Jan. 1961.

11. Mapleson, W. W.: The concentration of anaesthetics in closed circuits with special reference to halothane. I. Theoretical considerations, Brit. J. Anaes., 32:298-309, July 1960.

12. Morris, L. E., and Feldman, S. A.: Considerations in the design and function of anesthetic vaporizors, Anesthesiology, 19:642-649, Sept. 1959.

13. Mushin, W. W., and Galloon, S.: The concentration of anesthetics in closed circuits with special reference to halothane. III. Clinical aspects, Brit. J. Anaes., 32:324-333, July 1960.

14. Raventos, J.: The action of Fluothane, Brit. J. Pharm. and Chem., 11:394-410, Dec. 1956.

15. Robson, J. G., Gillies, D. M., Cullen, W. G., and Griffith, H. R.: Fluothane in a closed circuit, Anesthesiology, 20:251-260, May 1960.

16. Stephen, C. R., Lawrence, J. H., Fabian, L. W., Bourgeois-Gavardin, M., Dent, S., and Grosskreutz, D. C.: Clinical experience with Fluothane, 1,400 cases, Anesthesiology, 19:197-207, March 1958.